REMARKS

Claims 25-30 are pending. Claims 1-24 and 31 were previously canceled, without prejudice or disclaimer. Claims 25 and 26 have been amended as shown above to make explicit that the alphavirus replicon particles quantified using the claimed methods are replication defective. *See, e.g.,* paragraph 61 on page 18 of this specification. Claim 25 has also been amended to make explicit that the replicon particles produced in (c) are progeny of the replication defective alphavirus replicon particles in the contacting step (b), as described in paragraph 61. Because these amendments simply makes explicit what was previously implicit, no new matter has been added and entry thereof is requested. Thus, claims 25-30 are pending and stand rejected under 35 U.S.C. § 103.

Applicants request reconsideration of the application and withdrawal of the sole remaining rejection.

Request to Correct Inventorship Pursuant to 37 C.F.R. § 1.48(b)

In the response received by the Office on August 25, 2003, Applicants requested correction of inventorship pursuant to 37 CFR §1.48(b) to eliminate inventors who did not contribute to the currently pending claims. A check to cover the $130 fee was attached. Applicants respectfully inquire as to the status of their request to correct inventorship.

Rejections Under 35 U.S.C. § 103

All examined claims remain rejected as allegedly obvious over Dubensky. (Office Action, pages 2-3). In this regard, the Examiner again submitted that the comments made by Dr. John Polo (summarized in the previous Response) regarding Dubensky were unpersuasive:

> Applicant's substantive arguments are primarily directed to the supposed lack of teaching in Dubensky that alphavirus replicon particles are able to be enumerated by plaque assay (5,789,245, column 124, lines 11-21). Applicant argues that Dr. John Polo (an interested party in the present application and a co-inventor in 5,789,245) and co-inventors of the 5,789,245 patent did not even consider enumeration of alphavirus replicon particles by plaque assay at the time of the invention disclosed in 5,789,245.
>
> In response, Dr. Polo's remarks regarding the thoughts and intentions of the inventors of the Dubensky patent are not supported by the facts of record. The Office acknowledges that enumeration of alphavirus replicon particles by plaque assay was not possible because structural proteins were lacking (see, 5,789,245, column 124, lines 19-21). However the present claims are drawn to a method for

> quantitating alphavirus replicon particles produced in packaging cells which provide structural proteins. Dubensky teaches packaging cells containing expression cassettes that provide structural proteins. When Dubensky's vector construct is introduced into the packaging cells (col. 5, lines 64-66), the structural proteins are produced, allowing for the particles to be produced and detected by plaque assay (col. 19-20, bridging paragraph). Therefore, the presence of structural proteins allows for enumeration by plaque assay. Final Office Action, pages 2-3.

Applicants again traverse the rejection and supporting remarks.

For the reasons of record (reiterated below), the evidence of record is not at odds with the facts of record, as asserted by the Office. Rather, all of the evidence of record, including Dr. Polo's statements, is completely consistent with the fact that Dubensky does not suggest using plaque assays to quantitate replication defective alphavirus particles (and actually teaches away from such methods).

As a threshold matter, Applicants note that as a co-inventor of both Dubensky and the pending case, Dr. Polo is uniquely qualified to explain how the Dubensky reference fails to suggest the claimed methods to the skilled artisan. His explanations and opinions are based on intimate knowledge and understanding of both applications, including what Dubensky actually teaches with regard to use of plaque assays.

Moreover, Dr. Polo's statements are plainly supported by the other evidence of record, most notably Dubensky's own text, relevant portions of which are reproduced below. The record as a whole is clear that there are absolutely no teachings in Dubensky disclosing, suggesting or providing the motivation to arrive at the claimed methods. Dubensky teaches that plaque assays are useful **only** for titering levels of contaminating replication competent virus (also referred to as viable virus):

> Within the context of the present invention, the production of any measurable titer, for example, by plaque assay, luciferase assay, or beta-galactosidase activity of infectious virus on appropriate susceptible monolayers is considered to be production of **viable virus**. (Dubensky, col. 19, line 60 to col. 20, line 1, emphasis added).

Simply put, Dubensky refers to plaque assays solely in the context of titering replication competent virus.

Furthermore, the evidence of record belies the Examiner's contention that the claimed use of packaging cells (and therefore structural proteins) somehow makes the above-described

passage applicable to the pending claims. In reality, Dubensky is unambiguous that plaque assays cannot be used to titer replication defective particles, even when the particles are made using packaging cells:

> The titer of various alphavirus vector preparations, in vector units, **produced from packaging cell lines** such as those described in Example 7, is determined by infection of confluent monolayers of BHKSINjra-gal cells with several dilutions of vector. ... Since the alphavirus vectors described do not contain the viral region corresponding to the structural genes, it is **not possible** to determine titer of a vector preparation by plaque assay in BHK-21 cells. (Dubensky, col. 124, lines 11-21).

Thus, it is plain that Dubensky itself does not use plaque assays with to titer replication defective particles -- even when packaging cells containing structural proteins are used in production of replication defective particles. Accordingly, the evidence of record establishes that Dubensky teaches away from the claimed methods and, as such, cannot suggest the methods in which replication defective particles are titered by plaque assays.

It is well settled that the Office cannot pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. *In re Wesslau,* 47 USPQ 391 (CCPA 1965). Here, there is no connection or nexus set forth in Dubensky between methods of using plaque assays to titer viable virus and the distinctly more complicated methods used to titer replication defective particles, because it was thought plaque assays would not work for replication defective particles (*see, e.g.,* col. 124). Indeed, the difference between the plaque assays and other assays techniques (such as β-gal based techniques described in Dubensky) is not the presence or absence of packaging cells (see, col. 124 in which replication defective particles are in fact produced using packaging cells), but the fact that Dubensky did not think plaque assays would accurately or effectively titer replication defective virus.

In sum. because Dubensky teaches away from the claimed methods, the rejection appears to be based on improper picking and choosing of unrelated teachings from this reference and, as such, cannot be sustained.

CONCLUSION

In view of the foregoing, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

Please direct all further communications regarding this application to:

Marcella Lillis, Esq.
CHIRON CORPORATION
Intellectual Property - R440
P. O. Box 8097
Emeryville, CA 94662-8097.

Respectfully submitted,

Date: January 20, 2004

By: _____

Dahna S. Pasternak
Registration No. 41,411
Attorney for Applicants

CHIRON CORPORATION
Intellectual Property - R440
P. O. Box 8097
Emeryville, CA 94662-8097
Telephone: (510) 923-8406
Facsimile: (510) 655-3542